

# FIBROUS DYSPLASIA IN THE SPINE: PREVALENCE OF LESIONS AND ASSOCIATION WITH SCOLIOSIS

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**Background:** Lesions of fibrous dysplasia involving the spine and scoliosis are thought to be uncommon entities in patients with polyostotic fibrous dysplasia and McCune-Albright syndrome. By examining bone scans of a relatively large cohort of patients with these disorders, we sought to determine the prevalence of spinal involvement and any association with scoliosis.

**Methods:** Sixty-two patients with polyostotic fibrous dysplasia were studied. There were twenty-three male and thirty-nine female patients, and they had a mean age of twenty-five years (range, four to eighty years). Technetium-99m-methylene diphosphonate (MDP) bone scans of the patients were evaluated for evidence of increased uptake in the spine. The presence or absence of scoliosis or a level pelvis and the distribution of other lesions in the skeleton were noted.

**Results:** Thirty-nine (63%) of sixty-two patients were found to have seventy-six lesions of fibrous dysplasia in the spine. Fifty-four lesions (71%) demonstrated increased uptake in the posterior aspects of the spine. Most lesions were located in the lumbar spine (thirty-two lesions) and the thoracic spine (twenty-seven), with less frequent involvement in the sacrum (ten) and cervical spine (six). Twenty-five (40%) of the sixty-two patients had scoliosis; seventeen had a thoracolumbar curve; six, a lumbar curve; and two, a thoracic curve. Seven patients had curves that could not be accurately measured by bone scanning and, therefore, could not be classified. Thirty patients (48%) had no evidence of scoliosis. Thus, the prevalence of scoliosis in patients with polyostotic fibrous dysplasia was between 40% and 52%. There was a strong correlation between spinal lesions and scoliosis ( $p < 0.001$ ) and pelvic asymmetry ( $p < 0.05$ ). Back pain was an uncommon symptom. Two patients had a neurologic abnormality; neither abnormality was related to the location of the lesions or the curve.

**Conclusions:** Spinal lesions and scoliosis may be more common in patients with polyostotic fibrous dysplasia than has been previously reported. Since there is a strong correlation between a spinal lesion and scoliosis, these patients should be screened clinically for scoliosis.

**Level of Evidence:** Prognostic study, Level II-1 (retrospective study). See Instructions to Authors for a complete description of levels of evidence.

Fibrous dysplasia of bone is characterized by the replacement of bone and marrow with poorly organized spicules of immature bone in a fibrous connective tissue. The disorder, first described in 1938 by Lichtenstein<sup>1</sup>, was subsequently found to have monostotic and polyostotic varieties, the latter of which may be coupled with cutaneous and/or endocrine abnormalities (McCune-Albright syndrome)<sup>2,3</sup>. Overall, monostotic fibrous dysplasia is more common (80%) than polyostotic fibrous dysplasia (20%)<sup>4</sup>. Although fibrous dysplasia accounts for approximately 7% of all benign bone lesions, the prevalence of spinal involvement is thought to be very low, particularly in the monostotic form<sup>3,5-21</sup>. Fibrous dysplasia in-

volving the spine has also been seen in individuals with the McCune-Albright syndrome, and the prevalence has been reported to range from 7% in the cervical spine to 14% (five of thirty-seven patients) in the lumbar spine<sup>22</sup>. Isolated cases of patients who had malignant transformation of spinal lesions have also been reported<sup>4,23</sup>.

The prevalence of scoliosis in patients with polyostotic fibrous dysplasia and the McCune-Albright syndrome is not known. Guille and Bowen<sup>8</sup> reported on three patients with polyostotic fibrous dysplasia and scoliosis, two of whom required posterior arthrodesis. Janus et al.<sup>11</sup> reported the case of one such patient, who was also treated with posterior arthro-

TABLE I Clinical Characteristics of the Cohort

Diagnosis	No. of Patients	Gender (m/f)	Average Age (yr)	Endocrine Dysfunction (no. of Patients)	Café au Lait Lesion (midline) (no. of patients)
Polyostotic fibrous dysplasia	18	7/11	29.2	0	2
McCune-Albright syndrome	44	16/28	23.5	44	17

esis. Fibrous dysplasia both expands and weakens bone, resulting in structural changes. Although fibrous dysplasia involvement in the spine has been reported to cause changes in vertebral shape<sup>9</sup>, no correlation between the lesion location and the development of scoliosis has been described. Other anatomic considerations, such as limb-length discrepancy of the lower extremities or pelvic obliquity, which are also common in patients with fibrous dysplasia, may play a role in the etiology of scoliosis.

## Materials and Methods

### Patients

All patients provided written informed consent before enrollment in our long-term study of the natural history of polyostotic fibrous dysplasia or McCune-Albright syndrome, which was approved by the institutional review board. Enrollment in the study began in 1998, and two patients subsequently withdrew. The majority of the patients were recruited through a web site that described the natural history study and allowed individuals with polyostotic fibrous dysplasia to apply for enrollment in the study online. Additional patients were referred by their primary care physicians. The National Institutes of Health, as a research institution, would be expected to attract patients with a considerable amount of disease.

The study population consisted of sixty-two patients. There were twenty-three male and thirty-nine female patients, and the mean age was twenty-five years (range, four to eighty years). As part of the study, all patients had technetium-99m-

methylene diphosphonate (MDP) bone scans performed annually in order to track the location and activity of bone lesions. Whole-body bone scan images, made in the anterior and posterior planes with the patient in the supine position, were available for all patients. In addition, all patients had skeletal surveys of the pelvis and upper and lower extremities. When the protocol was first designed, radiographs of the spine were not included in order to remain within the allowable radiation quota for human subjects set by our institutional radiation safety committee. The decision not to include spine radiographs was made on the basis of the data in the available literature, which suggested that fibrous dysplasia involving the spine was an uncommon occurrence<sup>3,7,9,12,19-21,24</sup>.

### Bone Scan Measurements

The bone scan was used to determine the location of lesions in the cervical, thoracic, and lumbar spine and the sacrum, as well as the prevalence of scoliosis. The orientation of the pelvis was determined by assessing the angulation between the vertebrae in the lumbar spine and the line drawn across the top of the pelvis, and the pelvis was described as either level or not level with the shoulders. Lesions in the base of the skull, pelvis, long bones, and ribs were also recorded. Two different observers reviewed the bone scan data independently.

An estimate of the Cobb angle was performed with use of the end plates seen on the bone scan that yielded the largest magnitude of curvature. Actual Cobb angles were determined from spine or chest radiographs, made with the patient stand-

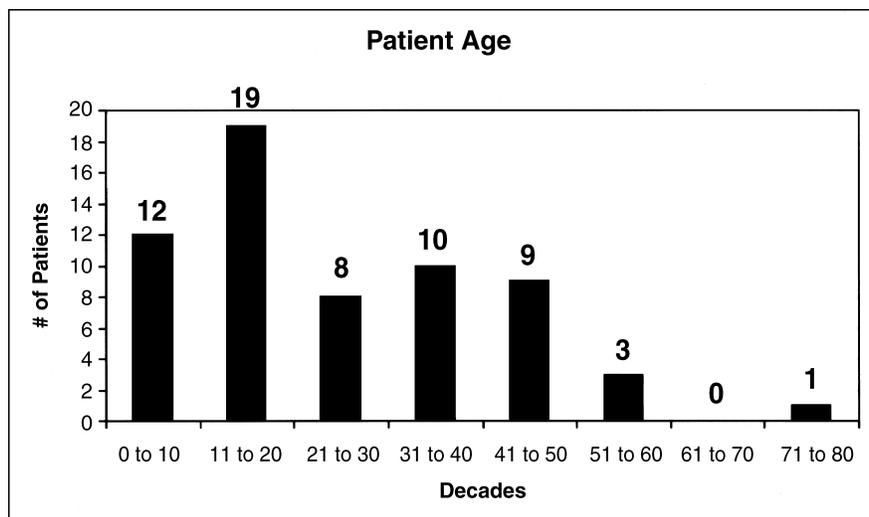


Fig. 1

Age distribution of the patient cohort.

ing, which were performed for eight patients for clinically indicated reasons. The difference between the estimated and actual angles in these eight patients was used to determine the degree of error in estimating Cobb angles from bone scans.

#### Other Testing

Patients underwent a comprehensive physical examination by an endocrinologist and a physiatrist on a yearly basis. Other specialists became involved in patient care as necessitated by the specific needs of each study patient. Patients were not routinely examined by either an orthopaedist or a neurologist; however, most of the patients were seen by a local orthopaedist whose records were incorporated into the patient's research chart. As a part of the study protocol, all patients had clinical photographs made to document skin lesions; blood analysis and urinalysis to assess for all of the endocrinopathies associated with polyostotic fibrous dysplasia or McCune-Albright syndrome, including precocious puberty, hyperthyroidism, acromegaly, hyperparathyroidism, and Cushing syndrome; and urinalysis to determine renal phosphate wasting (phosphaturia).

#### Statistical Analysis

Statistical analyses were performed with use of SAS software (version 6.12; SAS Institute, Cary, North Carolina). All numerically continuous parameters were summarized with use of means and standard deviations; means were compared with use of a one-way analysis of variance. Other analyses performed with SAS included Fisher exact tests and chi-square analyses.

#### Results

The clinical characterization of the patient cohort is summarized in Table I and Figure 1. Of the sixty-two study

patients, forty-four (71%) had McCune-Albright syndrome with multiple bone lesions, with or without *café au lait* spots, and with endocrinopathies, including precocious puberty, hyperthyroidism, acromegaly, and/or phosphaturia. The remaining eighteen patients had polyostotic fibrous dysplasia without endocrinopathy or phosphaturia (see Appendix). As we previously reported, the basic histological features of the biopsy specimens from patients with polyostotic fibrous dysplasia and the McCune-Albright syndrome were similar<sup>4</sup>.

An examination of the routine bone scans identified thirty-nine patients (63%) with seventy-six discrete lesions involving the spine. These lesions typically demonstrated increased tracer uptake. Fifty-four lesions (71%) were seen best in the scans made in the posterior plane for twenty-seven (69%) of the thirty-nine patients, while those made in the anterior plane demonstrated increased uptake in five patients (13%). Seven patients (18%) demonstrated extensive lesions in the scans made in both the anterior and posterior planes. When divided into groups on the basis of the different locations of the spine (cervical, thoracic, lumbar, and sacrum), twenty-eight patients (72%) had lesions that were localized to one or two anatomic sites, whereas the remaining nine patients (23%) had more extensive disease with three or all four anatomic locations involved (Fig. 2).

Patients were asked to report body pain at the time of initial enrollment, and few reported back pain. A complete neurologic examination was performed on all patients. One patient had neurologic changes attributable to basilar invagination, and another patient had a diagnosis of a peripheral neuropathy; the remaining sixty patients were neurologically intact. The spine was examined for scoliosis specifically by the physiatrist, but spinal deformity was not diagnosed in one-

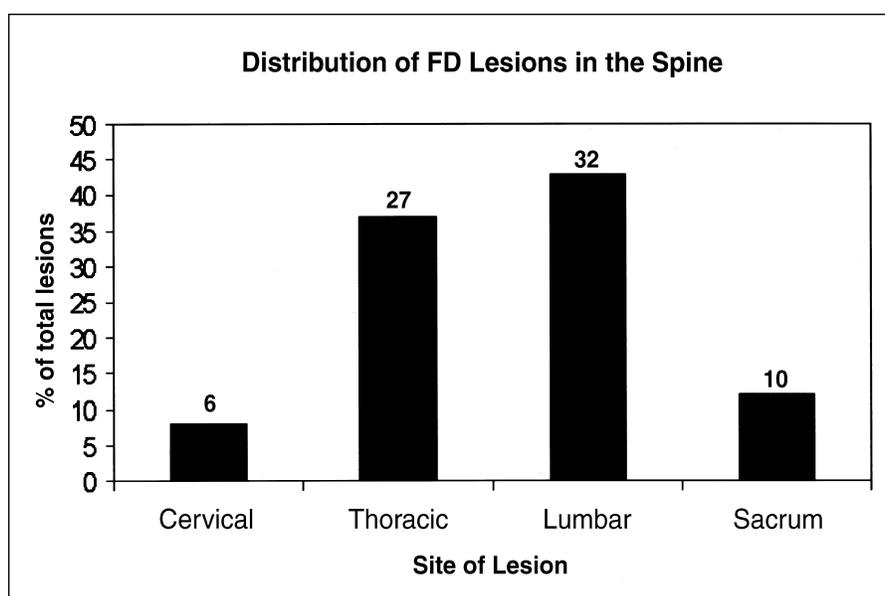
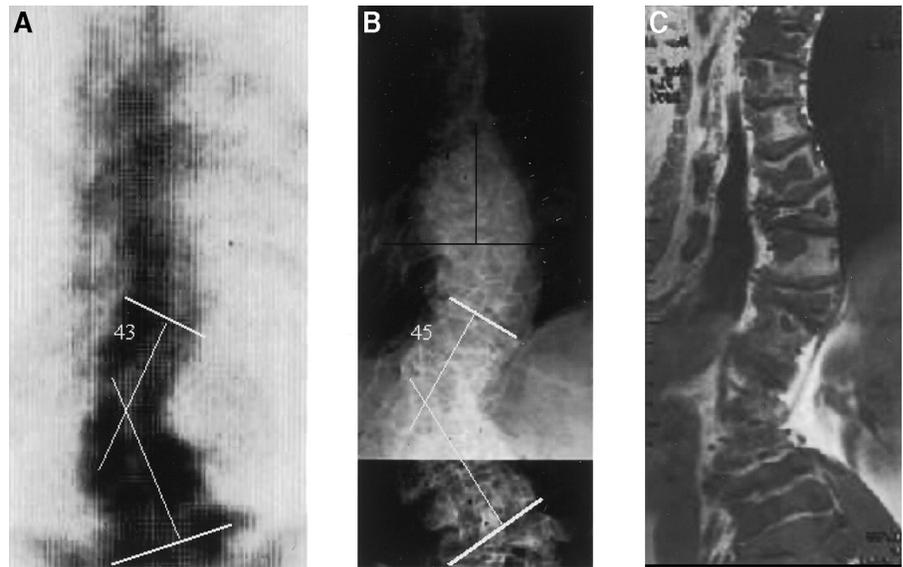


Fig. 2

Distribution of fibrous dysplasia (FD) lesions in the spine by location (lumbar, thoracic, sacral, and cervical spine).

Fig. 3

Bone scan (A), plain radiograph (B), and T2-weighted magnetic resonance image (C) of the spine of a patient with spinal fibrous dysplasia. The Cobb angles are demonstrated with use of both the bone scan and the plain radiograph. The magnetic resonance image shows the extent of replacement of normal bone with fibrous dysplasia.



fifth of the patients with scoliosis. Physical examination is particularly hard in these patients secondary to multiple deformities from involvement of fibrous dysplasia in the proximal part of the femora and the pelvis, in addition to that in the spine.

Although scoliosis is best determined radiographically, the high prevalence of spinal lesions in these patients prompted a closer evaluation of the patients for the presence of scoliosis. The possibility of using the bone scans to detect scoliosis was evaluated by a comparison of the estimated Cobb angles in the eight patients for whom both bone scans and plain radiographs were

available (Fig. 3). By comparing the values, we found that, in every case, the bone scan measurement underestimated the magnitude of the curve. The difference between the bone scan and the radiographic measurement ranged from 4.4% to 50.0%, with a percentage of error of  $27.7\% \pm 15.0\%$  (Fig. 4). Thus, although bone scan estimations are not very accurate in the measurement of scoliosis, they can be useful in the detection of spinal lesions that in turn correlate with the presence of a curve.

With use of the bone scan estimations, twenty-five (40%) of the sixty-two patients were identified as having a definitive

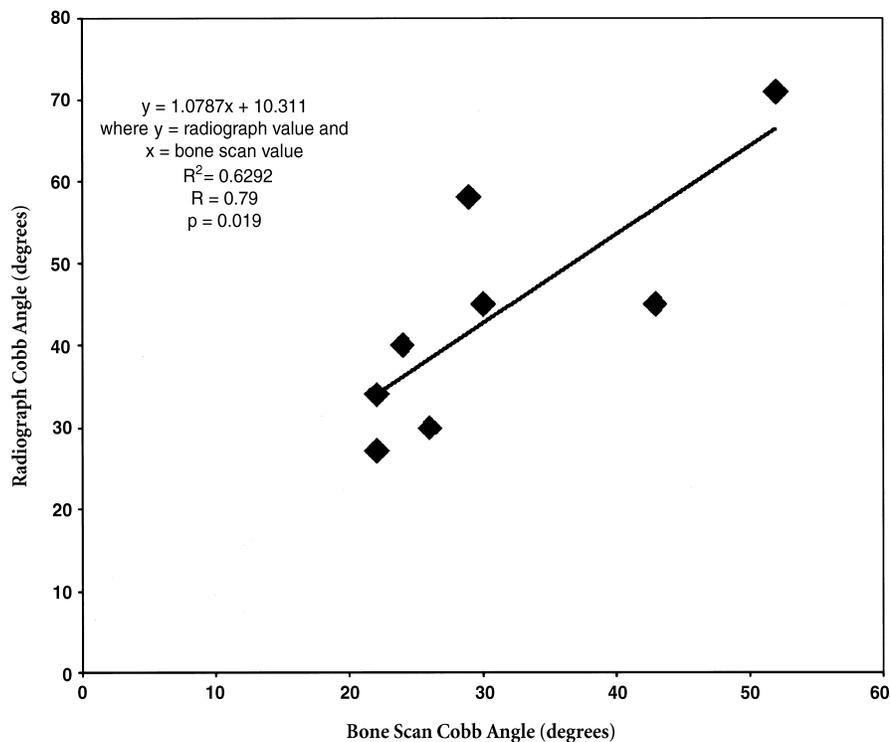


Fig. 4

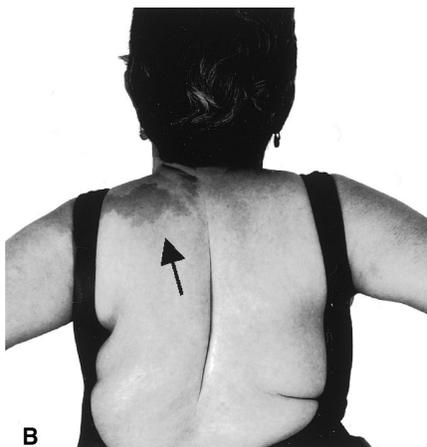
Graph showing the relationship between the measurement of the Cobb angle made on bone scans and that made on plain radiographs. The bone scan measurement of the Cobb angle underestimated the measurement made on plain radiographs.



A

Fig. 5

*Café au lait* spots. A: Midline lesions such as the one seen on the neck were located with proximity to the central axis of the body. B: Nonmidline lesions were located laterally away from the midline as in the lesion emphasized by the arrow.



B

scoliosis of  $>15^\circ$ ; thirty patients (48%) did not have scoliosis. The findings in the remaining seven patients (12%) could not be classified with regard to the presence or absence of scoliosis on the basis of the bone scan. These patients had an estimated Cobb angle measurement of between  $6^\circ$  and  $12^\circ$ , which is indeterminate because of the high percentage of error inherent in the bone scan measurement. Despite the imprecision of the estimated Cobb angle derived from a bone scan, these data demonstrated that the prevalence of scoliosis in this population of patients with polyostotic fibrous dysplasia and McCune-Albright syndrome is between 40% and 52% (if the indeterminate curves are all actual scoliotic curves).

The most common site of scoliosis was in the thoracolumbar spine (seventeen patients; 68%), followed by the lumbar spine (six patients; 24%) and the thoracic spine (two patients; 8%). Twenty-three (92%) of the twenty-five patients with definitive scoliosis had lesions of fibrous dysplasia contained within the confines of the curve, and only two patients (8%) had lesions outside the curve; the correlation between a spinal lesion and a curve was significant (Fisher exact test,  $p < 0.001$ ). Fourteen patients had spinal lesions without any evidence of curvature of the spine, and only two patients had scoliosis in the absence of fibrous dysplasia in the spine.

Four patients included in the analysis had posterior spinal arthrodesis and instrumentation with a variety of devices. All procedures were performed at other institutions. All of these patients underwent an uneventful arthrodesis with no evidence of loss of fixation or nonunion, on the basis of a review of their spine radiographs, at an average of twelve years (range, four to twenty-three years) of follow-up. While they were enrolled in the study, the four patients were monitored and showed no progression of the scoliosis after the spinal arthrodesis.

In the total population, we identified forty-six *café au lait* skin lesions (in patients both with and without endocrinopathy). We further classified a midline lesion as one that occurs centrally along the spine and a nonmidline lesion as one

that occurs lateral to the central axis of the body (Fig. 5). Nineteen patients (31%) had midline lesions, twenty-seven patients (44%) had lateral skin lesions, and the remaining sixteen patients (26%) did not have skin involvement. No correlation was found between a midline skin lesion and scoliosis.

Only one of the endocrinopathies, precocious puberty (thirty patients), correlated with the presence of lesions in the spine (Fisher exact test,  $p < 0.02$ ). Since precocious puberty can increase growth velocity, one would expect to see an increase in scoliosis in these patients, but no significant relationship was detected between precocious puberty and scoliosis. Instead, the presence of scoliosis appeared to be related to the presence of phosphaturia (twenty-two patients; Fisher exact test,  $p < 0.005$ ) and hyperparathyroidism (six patients; Fisher exact test,  $p < 0.01$ ). None of the other endocrinopathies appeared to be related either to the presence of lesions or to scoliosis; however, the number of patients in each group may have been too small to identify interactions.

For each patient, we also compared the presence of lesions in the long bones, pelvis, ribs, or base of the skull with the presence of lesions in the spine. However, with the numbers available, we found no correlation between lesion location in the spine and lesions in the long bones ( $p = 0.99$ ), pelvis ( $p = 0.26$ ), ribs ( $p = 0.35$ ), or base of the skull ( $p = 0.13$ ).

Since bone scans are performed with the patient in the supine position, they were also evaluated for the presence of a level pelvis. Nine patients (15%) had pelvic angulation from the midline of the spine, while the remaining fifty-three had a level pelvis. There was a significant correlation between the absence of a level pelvis and scoliosis ( $p < 0.05$ ).

## Discussion

On the basis of the findings of our study, involvement of fibrous dysplasia in the spine is more common than previously reported, with a prevalence of 63% in this group of patients with polyostotic fibrous dysplasia or McCune-Albright

syndrome. The bone scan data in the present study may, in fact, underestimate the true extent of disease since some areas of the spine can be obscured on the bone scan. For example, the anterior aspect of the cephalad thoracic spine is difficult to visualize under the sternum, and the mandible can cover the anterior aspect of the cervical spine. In addition, it is difficult to assign the precise location of lesions found at the rib-spine junction, which were designated rib lesions in this study but may actually represent involvement of fibrous dysplasia in the transverse processes.

While the prevalence of scoliosis could be estimated with use of bone scans, it was apparent that, for the eight patients who had both a bone scan and a plain radiograph, the bone scan consistently underestimated the degree of curvature. In addition, without radiographs, sagittal plane deformity such as kyphosis was missed. Anterior vertebral body disease may result in kyphotic deformity, which could not be measured on the bone scans, as no lateral scans were made. On the basis of the data from the bone scans and plain radiographs of the long bones of our cohort, we noted that all lesions of fibrous dysplasia on radiographs showed some increased uptake on bone scan. Thus, we are confident that we did not undercount lesions in the spine by examining the bone scan data. However, we intend to confirm this assumption with radiographs, computed tomography, and magnetic resonance imaging of our patients, a project currently underway. Nonetheless, the degree of spinal involvement detected by bone scanning is much higher than had been previously suspected, and this finding provides valuable information to clinicians concerning the need for evaluation of the spine in patients with polyostotic fibrous dysplasia and McCune-Albright syndrome.

For each patient, we noted lesions in the long bones, pelvis, ribs, or base of the skull to determine whether multiple sites of involvement in various anatomic areas are based on proximity. For example, do rib lesions and thoracic spine lesions, or a lesion in the sacrum and one in the pelvis, occur in combination? However, no association was found between spinal disease and lesions in other areas of the skeleton. The apparent random distribution of lesions in the body is thought to be related to the temporal and anatomic point during embryologic development when the missense mutation in the GNAS1 gene is introduced. Other studies have found that there also seems to be no relationship between the location of *café au lait* spots and the location of skeletal lesions<sup>1,22</sup>. Interestingly, we noted from the clinical photographs of our patients that very distinct *café au lait* spots were consistently located in the midline of the spine. These lesions were different from other lesions that stretched across the body laterally. However, separating midline skin lesions from all skin lesions did not reveal a correlation between midline lesions and spinal lesions in bone. We therefore cannot report any significant difference between the two types of skin lesions that we observed in terms of correlation of their presence with the presence of fibrous dysplasia in the spine.

The prevalence of both spine involvement and scoliosis

was higher than expected. Our findings indicate that bone scan data may be useful in determining when plain radiographs of the spine are needed for clinical management, especially for patients who are difficult to examine clinically because of deformities about the pelvis and lower extremities.

Also, as our study patients return for yearly follow-up examinations, they will undergo magnetic resonance imaging through the lesions in order to more accurately describe the anatomic location of the lesions, as well as the morphological characteristics of the vertebrae. Our cohort, who sought out a research protocol, may represent patients with a larger disease burden than those who are treated in the community at large, but this group will allow us to monitor the progression of scoliosis after skeletal maturity in these conditions.

The natural history of fibrous dysplasia of the spine is unknown. Many patients with polyostotic fibrous dysplasia have precocious puberty, which can result in the adolescent growth spurt occurring at an earlier age. Since scoliosis progresses during periods of rapid growth, it is possible that scoliosis occurs at an earlier age in patients with polyostotic fibrous dysplasia who have precocious puberty. Spinal deformity caused by vertebral deformity from replacement of bone with fibrous tissue may continue to progress into adulthood, and we hope that further study of fibrous dysplasia of the spine in our population will allow us to be able to determine the natural history of curve progression.

We believe that patients with polyostotic fibrous dysplasia need to be surveyed for spinal involvement, and that this is best accomplished by a bone scan. If lesions are found in the spine, then radiographs of the spine should be made, a detailed physical examination should be performed, and the individual should be closely monitored, and, if necessary, treated for scoliosis.

## Appendix

 A table showing specific data on all sixty-two patients is available with the electronic versions of this article, on our web site at [www.jbjs.org](http://www.jbjs.org) (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). ■

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